Contemporary Themes

Social and emotional complications in a clinical trial among adolescents with diabetes mellitus

A L KINMONTH, M K M LINDSAY, J D BAUM

Abstract

Observations are reported on the social and emotional events occurring among children with diabetes mellitus and their families while taking part in a demanding clinical trial. Participants were selected on the basis of: (1) age over 10 years, (2) "informed consent," (3) cooperation with diabetic care, and (4) family stability. Despite endeavours to apply these criteria, it subsequently emerged that one father had doubts about his daughter participating; one family was suffering from severe marital discord; a girl (11 years) and a boy (10 years) were unexpectedly distressed by the venepunctures required; and another girl (13 years) was falsifying the results of her urine tests. All the families wished to complete the trial, and only one did not because of recurrent hypoglycaemia. The psychosocial problems encountered during the trial were unpredictable and occurred despite selection. Documentation of these problems allowed appropriate emotional support to be offered to the children and their families and provided for a fuller and more reliable interpretation of the trial results than would have been possible from the numerical data alone.

Introduction

The rational management of diabetes mellitus and other chronic illnesses of childhood needs to be developed on the basis of controlled clinical trials. This inevitably means that children with chronic disorders must be asked to take part in research.[1] A demanding research protocol, however, may cause or exacerbate psychological problems. Moreover, events in normal life can reduce the ability of a family to follow a protocol accurately and so affect the results obtained, particularly in studies on diabetes mellitus, where a clear association exists between emotional distress and disordered metabolic control.[2 3]

We have attempted to describe the social and emotional problems reported by 11 diabetic children and their families who were participating in a demanding outpatient clinical trial.[4]

University Department of Paediatrics, John Radcliffe Hospital, Oxford OX3 9DU

A L KINMONTH, MA, MRCP, honorary registrar (diabetes)
J D BAUM, MD, FRCP, clinical reader in paediatrics

Child Guidance Clinic, Aylesbury, Bucks

M K M LINDSAY, MB, FRCPSYCH, consultant child psychiatrist

Correspondence to: Dr A L Kinmonth.

Methods

The clinical trial was approved by the hospital ethics committee. It consisted of a randomised within patient comparison of the effects of two contrasting diets on diabetic control and lasted three months. The protocol demanded strict dietary compliance and the regular collection of blood and urine samples. In addition, each child had a cannula inserted into an antecubital vein on two separate occasions during the trial for multiple blood sampling during a morning in the child's home.[4]

The research doctor (ALK) contacted families by telephone each week and visited them fortnightly to discuss problems arising from the medical protocol. Records were kept of all the domestic, social, and emotional events presented as problems by parents or children throughout the study.

STUDY POPULATION

Children were invited into the study on the basis of four criteria designed to exclude families who might find it difficult to cope with the demands of the trial. The children who were included had to be:

(1) Older than 10 years. This age was considered the earliest at which children could understand what was being asked of them and at which venepuncture might reasonably be attempted at home.

(2) Able, with both parents, to give "informed consent." Informed consent was defined as an agreement to take part in the trial after its implications had been explained by the research doctor in both group and individual discussions. The child, one parent, and research doctor all signed a consent form.

(3) Living in a stable family. This was defined as two parents living in apparent harmony with their children, as assessed by the family doctor, community nurse, and the consultant paediatrician (JDB).

(4) Showing a positive attitude to the care of their diabetes. This was defined as interest shown during outpatient consultations, together with compliance with urine testing for glucose and a carbohydrate regulated diet.

TABLE I—*Social and clinical characteristics of 11 children with diabetes mellitus selected for the dietary trial*

Child (name)*	Age (years)	Growth spurt (stage)	No of hobbies	Social class	Mother working	Duration of diabetes (years)	Diabetic control
Jack	11·3	A	2	3	Full time	2	Average
Malcolm	11·4	B	2	1	Part time	3	Average
Sam	11·7	A	2	3	Part time	1	Good
Michael	12·1	B	2	2	At home	2	Average
Celia	13·5	B	2	2	Part time	2	Poor
David	15·0	B	3	1	Part time	5	Average
Paul	15·5	C	2	2	Full time	14	Average
Terry	15·8	C	7	2	Full time	5	Average
Sarah	16·1	C	5	1	Full time	7	Poor
Joanna	16·1	C	5	2	Part time	4	Good
Diana	17·0	C	2	2	Full time	9	Good

A = Pregrowth spurt. B = Approaching peak height velocity. C = After peak height velocity.
Good = Glycosylated haemoglobin (HbA_1) $<10\%$. Average = HbA_1 10·1–12·0%. Poor = HbA_1 $>12\%$. (Normal reference 7·8%.)
*All names are fictitious.

Results

CHARACTERISTICS OF PARTICIPANTS

Eleven children took part in the trial and table I shows their clinical and social characteristics. The four girls and seven boys had a mean age of 14 years. Two children had not begun their adolescent growth spurt and nine had.[5] All the children were coping well with school work. In addition, they each engaged in a mean of three extracurricular school activities, ranging from games such as football, hockey, and swimming to singing, ballroom dancing, fencing, and flying. The occupational class of their families varied, but all the children except one had mothers who worked at least part time outside the home. The children had a mean duration of diabetes of five years, and there was a wide range of diabetic control as measured by glycosylated haemoglobin (HbA_1).[6]

LIMITATIONS OF SELECTION CRITERIA

Despite attempts to apply the selection criteria, four families took part who, in retrospect, should have been excluded (table II). All four families experienced difficulties during the trial as described below.

TABLE II—*Selection criteria not fulfilled in retrospect and unpredicted problems arising in nine out of 11 diabetic children during the clinical trial*

Child (name)*	Unfilled selection criteria			Unpredicted problems			
	Family stability	Cooperation with care	Family consent	Diabetic control	School	Child's health	Relation's health
Jack							
Malcolm					X		X
Sam		X					
Michael					X	X	X
Celia		X	X				X
David				X			
Paul					X		
Terry							X
Sarah							
Joanna	X			X		X	
Diana		X					

*All names are fictitious.

Case 1—Joanna was apparently a model teenager living in harmony with her mother, father, and older sister. She was head of her school and excelled at games; her diabetic control was good and she found the trial technically easy. After a month, however, she complained of weekend headaches and her blood glucose concentrations became less well controlled. The trial came to an end but Joanna's metabolic control did not improve, and she developed severe epigastric pain for which no physical cause was found. The family discussed these problems with the research doctor and the child psychiatrist attached to the clinic (ML). From these consultations it emerged that Joanna's parents had been separated for several years but were presenting a united front to the world. The very strong emotions released by this revelation were explored with apparent relief of anxiety symptoms. A year later, however, faced with leaving school Joanna required admission for psychiatric management of her depression and suicidal ideas.

Case 2—Sam was one of the youngest participants, with the shortest history of diabetes (table I) and was the only child in the trial not giving all his injections himself. He lived with his younger brother and parents and was a good all-rounder at school. As the trial progressed Sam protested with increasing vigour against the routine blood tests. Finally, when it was time to insert the intravenous cannula he burst into tears and locked himself in the lavatory. There he remained for 10 minutes until coaxed out by his brother and father. With continuing support from his parents (who in turn looked for support from the research doctor) he completed the trial.

Case 3—Diana, the oldest participant (table I) was a domestic science student. She had taken part in previous trials using blood sampling via indwelling cannulas. A week before the end of the trial Diana's mother told the research doctor privately that her daughter did not sleep the night before the doctor's visits to take blood and had cried with fear on some occasions. When this was discussed with Diana she agreed that she had a horror of blood tests but said that doing the project was more important to her than this fear. She completed the trial.

Case 4—Celia was the younger of two daughters and lived in a small village with her parents. Celia had always tried hard to please the clinic and persuaded her mother to let her join in the project. It was only later that we discovered that her father had strong reservations about this decision. Three weeks after beginning the trial Celia told her parents that she was breaking the experimental diet by eating chocolate at school. A sample of urine tested by her parents showed 5% glycosuria, although Celia had recorded it as negative. Celia's father rang the research doctor. He was concerned and angry, blaming the trial. Celia wished to continue with the trial, and her parents agreed. Subsequently, however, the mother rang frequently expressing loneliness in the responsibility of having allowed her daughter to engage in research against her husband's judgment.

UNPREDICTABLE PROBLEMS

Seven children suffered from unexpected problems during the trial (table II). These related to: diabetic control; school; and their own health or that of a close relative.

Diabetic control—Some problems with adjusting diabetic control were to be expected in a trial that included changes in treatment. In the case of David, the son of a scientist (table I), however, the diabetes was found to be so uncontrollable that the trial was stopped. His diabetic control measured by glycosylated haemoglobin (HbA_1) appeared to be average but early in the trial it emerged that this was at the expense of recurrent hypoglycaemic fits in the early morning. Attempts to avoid these by reducing the dose of insulin were associated with increasingly erratic blood glucose concentrations. The trial was stopped but the instability continued. A year later this was finally overcome by the use of an insulin infusion pump.[7]

School—Three children reported new or unexpected problems at school that interfered with the trial. Paul suffered ketoacidotic vomiting during exams; Malcolm became miserable and withdrawn for a month after starting his senior school; and Michael suffered misery at his mixed school because he was "teased by the girls."

Health—Seven of the 11 children had coughs or colds during the trial. Joanna and Michael had unexpected health problems; Joanna's abdominal pain has already been described. Michael presented as an emergency on Christmas day with chest pain for which there was no physical cause. He talked to the duty doctor about his feelings of loneliness since his grandmother died. He had been very attached to her, and this was the first Christmas they had not shared. Subsequent discussion with the research doctor resulted in Michael saying "he had got things off his chest" and he did not have the pain again. Three other children experienced illness among their close relatives during the trial. Malcolm's grandmother developed insulin dependent diabetes, Celia's grandfather had a minor stroke, and Terry's grandparents were both admitted to hospital with pneumonia.

PROBLEMS DUE TO FAMILY DYNAMICS

These children were growing up and becoming independent of their parents. Some parents tried to use the trial to maintain their authority while their children tried to use it to express their independence. Parents often asked the research doctor to discipline their children—for example, Paul's mother said, "I wish you would tell him not to lie about the house all day—it can't be good for him," and Sam's mother said, "I wish you would tell him to let us know where he's going—it's not safe for him to wander off."

On the other hand, the five older children tended to keep discussion with the research doctor entirely to themselves. For example, they did not transmit instructions about the diet to their mother, the family "cook."

Discussion

These observations illustrate the wide variety of domestic, social, and emotional events that occurred during a clinical trial and the effects these had on the children themselves. They indicate the extent to which such complications might be avoided or better managed in future studies.

Ten of the 11 families selected completed the trial. These families had certain group characteristics that might indicate an

ability to cope well. All the children enjoyed school and took part in several extracurricular activities; all but one mother worked outside the home. These findings suggest that busy families may cope well with added demands. They also suggest that a teacher's assessment might be useful in selecting children for clinical trials. All the children except Sam gave their own insulin injection. Such independence might be a more important sign of maturity among children with diabetes than age or compliance with urine tests alone.[8]

Although selection might be improved, the observations made show the limitations of selection criteria in avoiding psychosocial difficulties during research; in this trial it proved impossible to apply four simple selection criteria in all cases, and even obtaining written consent did not ensure that the whole family wished to take part.

Equally important, most problems presented were either unpredictable or unavoidable in children of this age group. Adolescence is accompanied by more changes than at any other time of life except infancy,[9] and diabetes tends to be unstable at this time.[10] It was impossible in this study to predict which child would have trouble with diabetic control, changing schools, taking exams, or coping with illness or death in the family.

We conclude that despite careful selection, children and adolescents in clinical trials will have social and emotional problems and these will be mainly unpredictable. Therefore, children and their families who are engaged in research will require continuing emotional support, and provision for the necessary support should perhaps be built into the design of such trials.

These observations illustrate the types of demands that families face when taking part in clinical research. Nevertheless, a description of the events making up the "normal life" under which the data of a trial are collected also provides an extra dimension for the scientific interpretation and clinical application of the results.

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Polychlorinated biphenyls are used as coolants in transformers. What treatment is advised when a person is contaminated as a result of a leak?

Polychlorinated biphenyls have the general structure shown (figure).

They are used commercially (Arochlor, Kanechlor, etc) as mixtures of polychlorinated biphenyls described in terms of percent chlorine. The materials range from oily liquids to waxy or hard solids, and because of their chemical stability and high dielectric constants they have been used extensively in electrical equipment as dielectrics and coolants. Polychlorinated biphenyls have also been used as heat exchange fluids, cutting fluid additives, and hydraulic fluids and in carbonless copy paper systems. Owing to evidence for their environmental stability and accumulation in the food chain, their use has been restricted to closed systems since 1971 in the United Kingdom and production here ceased entirely in 1977.[1] They are potent inducers of an acneform dermatitis, chloracne, known in various trades as cable rash. Lesions, normally papules and yellowish cysts surrounded by mild erythema, appear on the face, chest, abdomen, thighs, and buttocks. Comedones and pustules may develop later, and pruritus is common. Apparently polychlorinated biphenyls and chlorinated naphthalenes (which have similar toxicological properties) alter the differentiation of the sebaceous glands—keratinocytes form to plug the pilosebaceous unit creating cysts containing keratin.[2] They also cause irritation of the eye and transient visual disturbance.

Polychlorinated biphenyls are also hepatotoxic. In general oxides of polychlorinated biphenyls and higher degrees of chlorination are associated with higher toxicity. More highly substituted polychlorinated biphenyls are also retained longer in vivo. Symptoms of systemic intoxication, which include anorexia, nausea, vomiting, oedema, abdominal pain, and jaundice, usually occur some time after exposure, particularly after chronic exposure or when polychlorinated biphenyls are used in poorly ventilated areas. Deaths from toxic hepatitis have been reported.

The National Institute for Occupational Safety and Health (USA) has recommended the following procedures in the event of a leak or spill of polychlorinated biphenyls[3]; all non-essential personnel to be evacuated; adequate ventilation to prevent accumulation of vapours; clearing of the area; and the use of appropriate protective clothing and equipment. People occupationally exposed to polychlorinated biphenyls should work in well ventilated areas, wear protective clothing, have access to showers, and undergo periodic examinations of the skin and liver function tests. Barrier creams are of little use in controlling chloracne. If polychlorinated biphenyls are spilt on the skin the affected area should be washed thoroughly with soap and water for at least 15 minutes. If splashed in the eye the eye should be irrigated for at least 15 minutes. If chloracne develops exposure to polychlorinated biphenyls should cease. There is no evidence that chloracne responds to conventional treatment for acne, and ultraviolet or *x* radiation may exacerbate the rash. Damage to the liver and other features of systemic toxicity should be treated symptomatically.—G N VOLANS, director poisons unit, London.

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3 National Institute for Occupational Safety and Health. *Criteria for recommended standard. Occupational exposure to polychlorinated biphenyls.* Washington: NIOSH, 1977.

Corrections

Medical lessons from the Falklands

We regret that some errors appeared in the conference report by Dr Tessa Richards (5 March, p 790). The position of Port San Carlos and Ajax Bay should have appeared on the west coast of East Falkland. The dose of methylprednisolone should have been 2 g. HMS *Antelope* and *Coventry* were attacked by bombs and rockets but not by Exocet missiles.

Is weighing babies in clinics worth while?

We regret that in the Clinical Research edition an error occurred in figures 2 and 3 of this paper by Professor D P Davies and Dr T Williams (12 March, p 861). The figure shown above the legend to figure 2 should have appeared as figure 3 and vice versa.